

SUPPLEMENTAL MATERIAL

Supplemental Table: Peptide substrates of neprilysin relevant to cardiovascular and metabolic disease

Peptide	Cleavage sites	K_m (μM)	K_{cat} (min^{-1})	K_{cat}/K_m ($\text{min}^{-1} \mu\text{M}^{-1}$)	Ref
Angiotensin I	Asp-Arg- \downarrow Val-Tyr- \downarrow Ile-His-Pro- \downarrow Phe-His-Leu				1
Angiotensin II	Asp-Arg- \downarrow Val-Tyr- \downarrow Ile-His-Pro-Phe	280			1
ANP-28	Ser-Leu-Arg-Arg- \downarrow Ser-Ser-Cys- \downarrow Phe-Gly-Gly-Arg- \downarrow Met-Asp-Arg- \downarrow Ile-Gly- \downarrow Ala-Gln-Ser-Gly- \downarrow Leu-Gly-Cys-Asn-Ser- \downarrow Phe-Arg-Tyr	28.3	145	5.1	2,3
BNP-32	Ser-Pro-Lys-Met- \downarrow Val-Gln-Gly-Ser-Gly-Cys-Phe-Gly-Arg-Lys-Met- Asp-Arg-Arg- \downarrow Ile-Ser-Ser-Ser-Ser-Gly-Leu-Gly-Cys-Lys-Val-Leu- Arg-Arg-His	102	54.3	0.53	2
β-amyloid protein 42	Asp-Ala-Glu- \downarrow Phe-Arg-His-Asp-Ser-Gly-Tyr-Glu-Val-His-His-Gln- Lys-Leu-Val \downarrow -Phe-Phe-Ala-Glu-Asp-Val-Gly-Ser-Asn-Lys-Gly-Ala- Ile-Ile-Gly-Leu-Met-Val-Gly-Gly-Val-Val-Ile-Ala	2.8			4,5
Bradykinin	Arg-Pro-Pro-Gly- \downarrow Phe-Ser-Pro- \downarrow Phe-Arg	92.2	6364	69.0	6

CNP -22	Gly-Leu-Ser-Lys-Gly-Cys-↓Phe-Gly-↓Leu-Lys-↓Leu-Asp-Arg-↓Ile- Gly-Ser-↓Met-Ser-Gly-↓Leu-Gly-Cys	12.4	97.4	7.85	2
Endothelin 1	Cys-Ser-Cys-Ser-Ser-↓Leu-Met-Asp-Lys-Glu-Cys-Val-Tyr-Phe-Cys- His-↓Leu-Asp-↓Ile-Ile-Trp	2.3	131.4	57.1	7
Endothelin 2	Cys-Ser-Cys-Ser-Ser-Trp-Leu-Asp-Lys-Glu-Cys-Val-Tyr-Phe- Cys- His-↓Leu-Asp-↓Ile-Ile-Trp	10.7	221.0	20.7	7
Endothelin 3	Cys-Thr-Cys-↓Phe-Thr-Tyr-Lys-Asp-Lys-Glu-Cys-↓Val-Tyr-Tyr- Cys His-↓Leu-Asp-↓Ile-Ile-Trp	2.5	14.4	5.8	7
Gastrin (sulfated)	Pyr-Gly-Pro-Trp-↓Leu-Glu-Glu-Glu-Glu-Glu-Ala-↓Tyr(SO ₃ H)-Gly- ↓Trp-Met-Asp-↓Phe	57	46	1	8
Glucagon-like peptide 1 (7-36) amide	His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-↓Val-Ser-Ser-↓Tyr-↓Leu-Glu- Gly-Gln-Ala-Ala-Lys-Glu-↓Phe-↓Ile-Ala-Trp-↓Leu-Val-Lys-Gly-Arg- NH ₂				9
Insulin B chain	Phe-Val-Asn-Gln-His-↓Leu-CMCys-Gly-Ser-His-↓Leu-↓Val-Glu-Ala- ↓Leu-↓Tyr-↓Leu-↓Val-CMCys-Gly-Gly-Arg-Gly-↓Phe-↓Phe-↓Tyr-Thr- Pro-Lys-Ala	15	52	3.5	10,11

Proadrenomedullin N-terminal 20 peptide	Ala-Arg-↓Leu-Asp-Val-Ala-Ser-Glu-↓Phe-Arg-Lys-Lys-↓Trp-Asn-Lys-↓Trp-↓Ala-↓Leu-Ser-Arg	6.1			12
Substance P	Arg-Pro-Lys-Pro-Gln-Gln-↓Phe-↓Phe-Gly-↓Leu-Met-NH ₂	31.9	5062	158.7	6

ANP indicates atrial natriuretic peptide; BNP, brain natriuretic peptide; and CNP, C-type natriuretic peptide. Arrow (↓) indicates a cleavage site. For a complete list of peptide substrates of neprilysin see <http://merops.sanger.ac.uk/cgi-bin/substrates?id=M13.001>

K_m is the concentration of substrate needed to reach half maximum velocity; the lower the K_m the greater the affinity of the enzyme for the substrate. K_{cat}/K_m, or the specificity constant, conveys the relative rate of the enzyme neprilysin acting on the specific substrate.

Supplemental References

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